GUIDANT

TCT 2005
Thursday – Friday / October 20 – 21, 2005
Update

DRUG-ELUTING STENT SUMMIT

The "Disruptive" Impact of DES *Martin Leon*

- Suggested market maximum for DES in the US is 90%
- The total dollars in the global market will be no larger than it is today

Rapamycin Analog-Based Systems

ZoMaxx (Abbott)

- Abbott is having trouble enrolling patients in ZoMaxx II.
- Yeung showed impressive pre-clinical data showing Zotarolimus resembles Cypher in its inhibition of cell growth.
- Yeung showed pre-clinical data developed by Andy Carter that indicates that ZoMaxx is less inflammatory than Cypher after 90 and 180 days in porcine models. Yeung attributed this difference to the PC coating.

Xience

- Gregg Stone noted that the move from Champion was "problems with the Champion platform." Stone described the polymer in great detail – it is an acrylic and fluorinated polymer," described as "inert," "biocompatible," "easy to manufacture," "non-tacky," and "has good mechanical integrity."

INNOVATIVE DEVICES AND FUTURISTIC THERAPIES

- A couple of new and intriguing designs and overall, a movement towards disease specific solutions – this is something Campbell Rogers spoke about a few times during TCT.

Bifurcation Solutions

- The approach seems very consistent: stent the main vessel and leave yourself open to a case-to-case decision around side-branch treatment. Guidant seems very well-positioned to succeed here compared to the competition. The Tryton stent is an interesting concept but total metal is concerning. The SideKick device seems like a nice approach to side-branch-preservation with a wire.

Bioabsorbable Solutions

- Concluded that there is movement toward bioabsorbable solutions. Near-term with the polymer and long-term to completely absorbable platforms. A few different options were discussed in this section.

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VULNERABLE PLAQUE

- Continued trend of merging of non-invasive imaging and therapies
- First case reviews in a VP scientific symposium
  - Evidence the topic is becoming more clinically relevant
- Further endorsement of IVUS-based technology as the leading invasive VP diagnostic tools under investigation
- At least 4 natural history studies planned behind PROSPECT
  - Evidence of acceptance of concept of combining biomarkers and invasive imaging
- Very light on systemic therapies
- Serruys codified his screening / diagnostic cascade leading him to DES therapies for VP (first described at Euro PCR 2005)
- PREVAIL reincarnated as a 2,306 patient trial after talk of n = 300 pilot at VPM 2005

CONOR / BIOTRONIC EVENING SYMPOSIUM

- Two aspects of CoStar were promoted the most: minimal thrombogenecity and ability to deliver several drugs
- A number of CoStar's advantages were stated up-front:
  - Bioabsorbable polymer leading to the reduction of inflammation which in turn is likely to reduce the incidence of stent thrombosis. It was acknowledged that more than a year follow-up would be needed to make any definite statements about CoStar in this respect but there is "some data looking positive."
  - Deliverable stent with a very low profile. The stent was compared to Express, Bx Velocity, and Driver, and was presented as the most deliverable cobalt-chromium stent.
  - Reservoir technology making it possible to modify drug elution and applications. For instance, can use a reservoir system to deliver several drugs – currently evaluating paclitaxel and pimecrolimus. In animal studies, this particular combination has shown superior reduction in late loss.
  - All in all, the product was introduced as "safe, deliverable, and durable."

CLINICAL TRIALS

CYPHER

- New and positive CYPHER small vessel data was presented. The SIRIUS 2.25 registry data for expanded FDA approval was presented and had an 11.7% in stent and 16.9% in segment binary restenosis along with a low 4.3% TLR rate at 6 months with super small 2.04 mm vessels with 40% diabetics.
- The PORTO registry with 9 Portuguese hospitals demonstrated a even better CYPHER results with a 6.3% in stent 6 month binary restenosis and 8.2% TLR rate in 2.04 mm vessels in 100% diabetic patients.
- Buchbinder shared data from the DECODE study versus the BMS stenting in diabetics. This registry was halted prematurely due to favorable CYPHER results. Dr. Hyun-Sook of Korea presented preliminary data from a 3 Korean sites in a prospective randomized trial comparing CYPHER vs TAXUS in Diabetics. CYPHER is demonstrating an observed better results for CYPHER.
- CYPHER also had favorable 4.0 mm large vessel registry data for an expanded FDA indication with a low 2.2% in lesion binary restenosis rate and an 8.3% TLR rate.

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TAXUS

- TAXUS demonstrated good results in DIABETES II which was conducted in 4 sites in Spain as a follow-up to DIABETES I with CYPHER. In the first diabetic-only trial for TAXUS, it had a 0.33 mm in lesion late loss, 7.6% in lesion binary restenosis, and 7.5% TLR rate in 80 patients. The results were statistically better than in the bare metal control. Though the late loss was higher than CYPHER in DIABETES I, the binary restenosis and TLR rates were almost identical.
    - Dr. Corros was grilled following this presentation regarding this data and his core lab because the TAXUS late loss did not follow the signature Paclitaxel pattern now seen in so many studies. So, with all this new diabetic data at TCT, what is the net out? To date, ISAR DIABETES remains the most robust trial using a prospective, randomized design and demonstrating statistically better results for CYPHER over TAXUS in diabetics.
- Dr. Columbo presented the preliminary TRUE Taxus Web-based Registry data with over 1,000 patients in a real world setting with low 11.5% TLR rate.
- Mary Russell presented the Wisdom OUS post market, MILESTONE II OUS real world with diabetic focus, and ARRIVE I U.S. Peri-approval Web-based results. The TLR rates were all favorable in these Internet studies. In all of these Internet studies, there was only a low percentage of patients that were audited, and in the audited patients an overwhelming number of the total reported events were found, causing concern over the true event rates of these internet type registries.
- New TAXUS AMI data was presented in the PASSION study from 2 centers in Holland. In 311 AMI patients, TAXUS did have a low 1% TLR and 7.6% MACE rate in patients with a 3.13 mm vessel. But, overall most presenters stated that DES stenting in an AMI setting still requires more data which is currently being collected.

LATE-BREAKING CLINICAL TRIAL UPDATES: REGISTRIES

CHINA CYPHER SELECT REGISTRY

- A post-market surveillance to monitor safety and reliability and the ability to match trial results in a clinical environment, with an endpoint of TLR at 12 months.
- Conclusion: The endpoint has yet to be reached but the goal is 100% follow-up of 1,189 patients.
- Dr. Ormiston's commentary pointed out that registries have good "real life" information but the limitations of subjectivity.

EVENT

- Multi-center registry of the practice and outcomes of PCI in the DES era, done in 2 waves, 1 involves 2,537 patients, 31 sites, plus an additional 11 sites in wave 2.
- Conclusions: Wave 1, with 92% DES, ischemia and bleeding complications remained uncommon, and pre-procedure Troponin elevation is common, 6 month outcomes were favorable.

STENT

- A centralized database of 8 centers representing a "real world" view of cases, from May 2004 – September 2004 (SES not available until March 2004) consenting 8,000 – 10,000 cases per year
- Conclusions: There is no statistical difference between treatments with SES or PES – they have comparable clinical and safety outcomes.

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TCT 2005
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Update

AXXESS PLUS

- Non-randomized 125 patient multi-center, comparison of Axxess, self-expanding nitinol stent, coated with bioabsorbable PLA polymer with Biolimus A-9 for bifurcations vs. BMS Axxess stent. Primary endpoint of in-stent late loss at 6 months.
- Conclusion: First side-branch restenosis rate <10%, met primary endpoint at 5.6% in stent restenosis.

CREATE

- Study regarding carotid stenting with the use of Spider Distal protection with 419 high-risk patients.
- Conclusion: Late events (7.4% death) were due to high-risk profile of patients with serious comorbidities, not stroke

CAPTURE

- An evaluation of carotid stenting in community practice. Maximum of 40 patients per center with a mix of experience of the physicians and hospital.
- Conclusion: Patients under 80 years old responded extremely well, regardless of the level of experience of the physician, as compared with Archer trial, when training is available.
- The commentator, Dr. Gray, also felt this type of data would help with reimbursement efforts.

THANK YOU TO THE SESSION COVERAGE TEAM

- Aimee Angel
- Amy Belt
- Jon Bixler
- Monique Caruth
- Victoria Danilchouk
- Susan Feldmeir
- Christine Fernandez
- Anne Gildersleeve
- Andy Glass
- Joel Haaf
- Bob Jones
- Gail Pedrick
- Carlena Robison
- Natasja Romijn
- Matt Schmidt
- Leslie Stephens
- Andrew Tochterman

From: Myrdal, Kay L
Sent: Friday, February 10, 2006 2:41 PM
To: Simhambhatla, Murthy V
Subject: RE: Rome Breakfast meeting

Here's something to think about in your presentation...

"VISIONARY PERFORMANCE is the next level of performance which means not compromising on Deliverability, Efficacy or Safety. XIENCE V achieves VISIONARY PERFORMANCE by taking VISION, the proven MULTI-LINK platform, to VISIONARY with the integration of the state-of-the-art drug Everolimus and biocompatible polymer."

Kay

From: Simhambhatla, Murthy (SC)
Sent: Friday, February 10, 2006 11:16 AM
To: Myrdal, Kay (SC)
Subject: RE: Rome Breakfast meeting

Kay,

I liked your "no compromises" message to distinguish Xience as a next-gen system. Perhaps I can work that into my presentation verbally. Let me know if you have other thoughts on key positioning messages to deliver.

Thanks,
Murthy

From: Myrdal, Kay (SC)
Sent: Friday, February 10, 2006 8:33 AM
To: Coro, Gianni (MIL); Simhambhatla, Murthy (SC)
Cc: Comprensore, Cristina (MIL); Torrisi, Giuseppe (MIL); Bhargava, Anurag (BRU); Saint Girons, Pierre (BRU); Calle Gordo, Jose (Pepe) (BRU); Belt, Amy (SC); French, Fritz (SC)
Subject: RE: Rome Breakfast meeting

Gianni:

The agenda will be split out as Pepe suggested in a previous email:

Technical/Product Development Presentation - Murthy - this presentation has already been developed by me

Pre-Clinical and Clinical Data Presentation - Dr Stone

Q&A

Amy Belt from my team has already been in contact with Dr. Stone and has a provided an outline for him to follow. Dr. Stone has over 150 slides on Xience V from which to choose. I don't think you need to contact him.

Thanks

Kay

From: Coro, Gianni (MIL)
Sent: Friday, February 10, 2006 8:20 AM
To: Simhambhatla, Murthy (SC)
Cc: Comprensore, Cristina (MIL); Torrisi, Giuseppe (MIL); Myrdal, Kay (SC); Bhargava, Anurag (BRU); Saint Girons, Pierre (BRU); Calle Gordo, Jose (Pepe) (BRU)
Subject: Rome Breakfast meeting

Dear Murthy,

we are finalizing the agenda for the Breakfast meeting in Rome, the title will be: "Why Xience V can be a second generation DES" , there will be a brief introduction by our country manager Giuseppe Torrisi, and we will like to have a description of the argument that Dr.Stone and you will treat, in order to have an agenda, did you discuss this with Dr.Stone? have we to contact him directly?

Thank you for your collaboration

Gianni

Gianni Corò
VI Brand Manager
tel.: +39 02 26983276
cell.: +39 348 2512727

Da: Myrdal, Kay (SC)
Inviato: giovedì 9 febbraio 2006 1.15
A: Coro, Gianni (MIL)
Cc: Comprensore, Cristina (MIL); Torrisi, Giuseppe (MIL); Simhambhatla, Murthy (SC); Calle Gordo, Jose (Pepe) (BRU); Saint Girons, Pierre (BRU); Bhargava, Anurag (BRU)
Oggetto: RE: Dear Greg,

Dear Gianni:

Thanks for your message. We typically pay Gregg Stone $1,500 for a speaking engagement at a congress even when he is already in attendance.

As for the promotional video, Pierre Saint Girons and his marketing team are preparing the video for the XIENCE V launch in Europe. Please contact either Pierre or Anurag to obtain a copy.

Best Regards,

Kay

From: Coro, Gianni (MIL)
Sent: Tuesday, February 07, 2006 9:39 AM
To: Myrdal, Kay (SC)
Cc: Comprensore, Cristina (MIL); Torrisi, Giuseppe (MIL); Simhambhatla, Murthy (SC); Calle Gordo, Jose (Pepe) (BRU)
Subject: R: Dear Greg,

Dear Kay,

thanks for your involvement in this initiative, we are sending all the details to Dr.Stone, included his honorarium. Referring to this, we usually pay an amount of about 1.000$, considering that Dr.Stone is already in Rome for the Congress, do you think that this amount will be appropriate for him?

Pepe told me that you and your group are preparing a promotional video on Xience V for external use, do you think that will be possible to show it during the JIM Congress?

Waiting for your comments I thank you for your collaboration.

Best regards.

Gianni

Gianni Corò
VI Brand Manager
tel.: +39 02 26983276

cell.: +39 348 2512727

Da: Calle Gordo, Jose (Pepe) (BRU)
Inviato: mercoledì 1 febbraio 2006 19.57
A: 'Gregg W. Stone MD (gstone@crf.org)'
Cc: 'ggallo@crf.org'; Torrisi, Giuseppe (MIL); Coro, Gianni (MIL); Simhambhatla, Murthy (SC); Myrdal, Kay (SC); Chiarin, Massimo (MIL)
Oggetto: Dear Greg,

Great to hear back from you.

I just spoke with the Italian Guidant group and got confirmation from them about the breakfast meeting on Friday Feb 17, 7:00am-8:00 am at the Congress Hotel (Cavaliere Hilton in Rome).

As I mentioned briefly on the phone, the idea is to organize a breakfast meeting with some 20-30 top Italian interventional cardiologists to share with them some more insights into the Guidant Xience V program (why Xience V can be a second generation DES). You being so closely involved with my former team in Santa Clara and being the PI of SPIRIT III, are the most indicated person to help us with this initiative.

Joining you will be Murthy Simhambhatla (VP Product Development DES). I think you have met him in past Advisory Board meetings or in Santa Clara.
I will ask the Santa Clara folks to coordinate directly with you with regards to how to organize the details of the session and supporting you with slides/materials. (who talks about what?)

Giuseppe Torrisi and Gianni Coro from the Italian organization are setting up the logistics. They will invite the physicians, and set up the logistics for the session (breakfast, room etc). Of course they will also provide you with an honorary for your contribution to this talk.

Thanks again for accepting this invitation given the short notice. Having received CE mark only two days ago and getting closer to the commercialization in Europe., it is an opportunity for all of us to start being more vocal about the Xience V.

Looking forward to seeing you in Rome. I will most likely arrive on Feb 16 in the morning. If you don't have specific plans for dinner that evening I would be more than happy to invite you to dinner. Let me know.

Regards
Pepe

Jose Calle
Vice President Marketing Guidant EMEAC
Phone +32 2 714 1503
Cell +32 478 870 153

February 10, 2006

Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, MD 20850

RE: Supplement to IDE G050050 (XIENCE™ V Everolimus Eluting Coronary Stent System): Continued Access (SPIRIT IV) Clinical Trial

Dear Sir/Madam:

Please find enclosed a supplement for the XIENCE™ V Everolimus Eluting Coronary Stent System (EECSS). In accordance with the FDA Blue Book Memorandum D96-1 (Continued Access to Investigational Devices During PMA Preparation and Review), Guidant is submitting this IDE supplement to request FDA approval for continued enrollment of subjects, in a separate clinical trial, following the enrollment completion of the SPIRIT III clinical trial (i.e., the on-going controlled clinical trial under IDE G050050). Approval of this IDE supplement will allow continued access to the XIENCE™ V EECSS medical device while the marketing application is being prepared by Guidant. Consistent with the nomenclature of previous XIENCE™ V EECSS clinical studies, the continued access clinical trial will be referred to as the "SPIRIT IV" trial. Guidant believes the preliminary evidence from all animal safety studies and human clinical studies indicate that the device will be effective and there are no significant safety concerns.

The purpose of the SPIRIT IV Clinical Trial is two fold:

- To further evaluate the safety and efficacy of the XIENCE™ V Everolimus Eluting Coronary Stent System.
- If necessary, to enroll SPIRIT III-like subjects in order to support the SPIRIT III major secondary endpoint (270 d TVF), via the adaptive design methodology.

The SPIRIT IV Clinical Trial will enroll approximately 1,125 subjects at up to 50 sites in the United States. This trial will be randomized (2:1 XIENCE™ V EECS : TAXUS EXPRESS^2 PECS) in subjects with a maximum of three *de novo* native coronary artery lesions, maximum of two lesions per epicardial vessel with reference vessel diameters (RVD) $\geq$ 2.5 mm to $\leq$ 4.25 mm, lesion lengths $\leq$ 28 mm. Overlapping stents will be allowed for XIENCE™ V subjects with lesions > 22 mm.

As of February 7, 2006, a total of 1,230 subjects have been enrolled in the SPIRIT family of trials. Guidant believes there is sufficient justification to initiate the SPIRIT IV Clinical Trial to continue to evaluate the safety and efficacy of XIENCE™ V EECSS.

The results of the SPIRIT FIRST Clinical Trial at 1-year and DSMB recommendations to continue the clinical evaluations as planned for the SPIRIT II and III Clinical Trials, which are provided in this supplement support the safety and potential efficacy of the XIENCE™ V EECSS.

SPIRIT IV will be initiated with product made under the current manufacturing processes (EtO cycle 15). However, Guidant intends to introduce process changes including stent retention optimization and EtO sterilization cycle 100 which will be submitted in subsequent IDE supplements for FDA approval prior to implementation..

In an effort to provide clarity, Guidant has appropriately updated sections of the IDE to incorporate the relevant clarifications, corrections, or updated information related to the SPIRIT IV trial.

Note that the numbering of the sections remains consistent with the section numbers provided in the original IDE, with the exception that Data Safety Monitoring Board (DSMB) and Clinical Events Classification (CEC) have been added as sections 2.7.7 and 2.7.8, respectively. Therefore, the Bibliography and Copies of Referenced Papers has now become 2.7.9 (previously indicated as 2.7.7 in the IDE).

Thank you in advance for your review of this supplement for the XIENCE™ V EECSS. If you have any questions or require additional information regarding the SPIRIT IV portion of this supplement, please contact me at (408) 845-1374 or Jennifer Mateus, Manager of Regulatory Affairs at (408) 845-1316.

Sincerely,

Richelle Faria
Regulatory Affairs Associate

Enclosure

PART I: Continued Access

In accordance with the FDA Blue Book Memorandum D96-1 (Continued Access to Investigational Devices During PMA Preparation and Review), Guidant is submitting this IDE supplement to request FDA approval for continued enrollment of subjects, in a separate clinical trial, following the enrollment completion of the SPIRIT III clinical trial (i.e., the on-going controlled clinical trial under IDE G050050). Approval of this IDE supplement will allow continued access to the XIENCE™ V EECSS medical device while the marketing application is being prepared by Guidant. Consistent with the nomenclature of previous XIENCE™ V EECSS clinical studies, the continued access clinical trial will be referred to as the "SPIRIT IV" trial. Guidant believes the preliminary evidence from all animal safety studies and human clinical studies indicate that the device will be effective and there are no significant safety concerns (see below). The information provided in this section includes the following:

- Overview of the On-going SPIRIT Clinical Trials;
- A Summary of the Safety and Effectiveness Data to Support the Initiation of SPIRIT IV;
- A Discussion of the Risks Posed by the Device;
- The Proposed Rate of Continued Enrollment;
- A Summary of the SPIRIT IV Clinical Protocol;
- Marketing Approval Status of the XIENCE™ V EECSS.

1.0 Overview of the On-going SPIRIT Clinical Trials

Guidant is currently investigating the XIENCE™ V EECSS in the following trials:

Table 1-1: Current Clinical Trial Comparison

	SPIRIT FIRST	SPIRIT II	SPIRIT III
Study Type	Feasibility and Performance	Continuation in Assessment of Safety and Performance	Safety and Efficacy
	Multi-center (N=9), prospective, randomized, controlled, single-blinded, parallel two-arm (Europe)	Multi-center (N=28), prospective, randomized, active controlled, single blinded, parallel two-arm (International)	Multi-center (US sites: 80) RCT: randomized, active controlled, single blinded, parallel two arm RCT with 3 concurrent non randomized arms (Japan sites: 12): non randomized arm (US & Japan)

	SPIRIT FIRST	SPIRIT II	SPIRIT III
Number of Subjects	60 (28 XIENCE™ V, 32 Control)	300 (225 XIENCE™ V, 75 TAXUS® PECS)	Total N=1380 (US: 1292) RCT Arm: 1002 (668 XIENCE V: 334 TAXUS® PECS) (2:1 randomization XIENCE V arm to TAXUS arm) Angiographic subgroup: N=564 IVUS subgroup: N=240 4.0 mm Arm: 80 2.25 mm Arm: 105 38 mm Arm: 105 Japan Arm: 88
Lesion Criteria	*De novo* lesion in native coronary artery, RVD ≥ 2.8 mm to ≤ 3.2 mm, lesion length ≤ 12 mm	Maximum of two *de novo* native coronary artery lesions in two different epicardial vessels, RVD 2.5 mm to 4.25 mm, lesion length ≤ 28 mm; overlapping stents allowed for XIENCE V subjects with lesion lengths > 22 mm	Maximum of two *de novo* native coronary artery lesions, each in a different epicardial vessel, Arm RVD (mm) LL (mm) RCT 2.5 - 3.75 ≤ 28* 2.25 2.25 - 2.5 ≤ 22 4.0 3.75 - 4.25 ≤ 28* 38 3.0 - 4.25 > 24 - ≤ 32 Japan 2.25 - 4.25 ≤ 28* *Overlapping stents allowed for XIENCE V subjects with lesion lengths > 22 mm to ≤ 28 mm
Device Products Used	XIENCE™ V EECSS (Test) and MULTI-LINK VISION® RX CSS (control)	XIENCE™ V EECSS System (Test); Non-inferiority to TAXUS® PECS System	XIENCE™ V EECSS System (Test); Non-inferiority to TAXUS® PECS System
Antiplatelet Therapy	Protocol prescribed regimen: Aspirin for 1 year, and clopidogrel or ticlopidine for 3 months	Protocol prescribed regimen: Aspirin for 1 year and clopidogrel or ticlopidine for 6 months	Protocol prescribed regimen: Aspirin for 5 years and clopidogrel for 6 months (all subjects); Ticlopidine (per standard of care) for Japanese subjects and for subjects with clopidogrel allergy

	SPIRIT FIRST	SPIRIT II	SPIRIT III
Follow-up	30-day clinical; 180-day clinical, angiographic, IVUS; 270-day clinical (phone/office); 365-day clinical, angiographic, IVUS; up to 5-year clinical (phone/office)	30-day clinical; 180-day clinical, angiographic, IVUS; 270-day clinical (phone/office); 365-day clinical; 2-year clinical; 2-year angiographic and IVUS for a subset of 152 subjects at selected sites	30-day clinical (office visit); 180-day clinical (phone/office); 240-day angio/IVUS/clinical (hospital/office) 270-day clinical (phone/office); 1-5 yearr- clinical (phone/office)
Trial Status	Enrollment Complete on April 1, 2004	Enrollment Complete on November 10, 2005	As of Feb. 7, 2006 US RCT: 811 US 2.25 mm: enrollment not started yet. US 4.0 mm: 50 US 38 mm: enrollment not started yet. JPN: 9 US PK: 11 JPN PK: 4

In addition to the clinical trials presented above, Guidant intends to conduct a European post-market surveillance study called SPIRIT V. The clinical study protocol is under development. The preliminary study design of SPIRIT V will consist of two studies, the SPIRIT V Diabetic Study and the SPIRIT V Registry. In the SPIRIT V Diabetic Study, 321 subjects will recruited at 30 selected sites. They will be randomly assigned to receive either a XIENCE™ V EECSS or a TAXUS® Liberté™ stent. These subjects will have angiographic follow-up at 270 days, and clinical follow-up at 30 days, 8, 12 and 24 months. The SPIRIT V Registry will be a post-approval study involving up to 100 sites worldwide, and several thousands subjects will be recruited. All registry subjects will have clinical follow-up at 30 days, 12 and 24 months.

Additional details on the ongoing SPIRIT clinical trials are provided in PART II: Updated Sections of the IDE (G050050) Section 2.6 of this supplement.

2.0 Summary of Safety and Effectiveness to Support the Initiation of SPIRIT IV

As of February 7, 2006, a total of 1,230 subjects have been enrolled in the SPIRIT family of trials. Guidant believes there is sufficient justification to initiate the SPIRIT IV Clinical Trial to continue to evaluate the safety and efficacy of XIENCE™ V EECSS. The results of the SPIRIT FIRST Clinical Trial at 1-year and DSMB recommendations to continue the clinical evaluations as planned for the SPIRIT II and III Clinical Trials and support the safety and potential efficacy of the XIENCE™ V EECSS. Below please find a brief summary of the safety and effectiveness data to support the initiation of SPIRIT IV.

2.1 SPIRIT FIRST

The SPIRIT FIRST clinical trial represents the first clinical evaluation of the Guidant XIENCE™ V Everolimus Eluting Coronary Stent System, which evaluated the potential benefits of the local application of Everolimus in combination with a thinner strut stent design. Referred to as the MULTI-LINK VISION-E™ STENT in this summary and in the SPIRIT FIRST Report.

A total of 60 trial subjects with single, *de novo*, native coronary lesions who provided signed informed consent were enrolled between December 16, 2003 and April 1, 2004. Subjects were randomly assigned in a 1:1 ratio to one of the two treatment arms (28 subjects were enrolled in the test arm and received the Guidant XIENCE™ V EECSS, and 32 subjects were enrolled in the control arm and received the Guidant MULTI-LINK VISION® stent).

The SPIRIT FIRST Trial one year follow-up demonstrated that the treatment effect that was observed at 6 month was sustained at 1 year for the ML VISION Everolimus Eluting Stent. The ML VISION-E™ arm one year in-stent late loss of 0.23 mm represented a 72% reduction in late loss as compared to the control. The one year in-segment late loss of 0.13 mm represented a 78% percent reduction in late loss compared to the control. This was matched by low proximal and distal late loss values of 0.14 mm and 0.03 mm, respectively, indicating no cause for concern regarding edge effects.

Evaluation of the changes in in-stent MLD over time (post procedure, 6 and 12 months) showed that the treatment effect was sustained over the one year period. There was only a slight decrease in in-stent MLD (0.12 mm) which was associated with a clinically irrelevant increase in %DS (1.62%). Similar results were shown with in-segment MLD. Thus the treatment effect observed at 6 months for the ML VISION-E™ was maintained at one year.

These observations were consistent with IVUS measurements. The one year results showed a reduction of neo-intimal volume by 60% as compared to control. A small decrease in percent of volume that was NOT obstructed (1-%VO) was observed from 6 to 12 months and is considered clinically insignificant.

Therefore both the angiographic and IVUS measurements show that the patency of the ML VISION-E™ treated vessels was maintained throughout the year.

The clinical safety observed at 6 months was sustained at 1 year as demonstrated by no observations of late stent thrombotic events, no instances of late acquired stent malapposition, and only 1 out of 26 subjects with device related MACE.

The first year report available in **Appendix I** details data derived from the analysis of the 270-day clinical follow-up and 1-year clinical and angiographic/IVUS follow-up of the trial's subjects.

2.2 SPIRIT II Clinical Trial

The SPIRIT II European clinical trial was designed to continue the assessment of safety and performance of the XIENCE™ V EECSS.

A total of 300 trial subjects with a maximum of two *de novo* native coronary artery lesions in two different epicardial vessels were enrolled between July 5, 2005 and November 10, 2005. Subjects were put into one of the two treatment arms: the test arm (XIENCE™ V EECSS), or the Active Control arm (TAXUS™ EPECSS); patients were randomized 3:1 (XIENCE™ V EECSS: TAXUS™ EPECSS). A total of 225 subjects received the XIENCE™ V and 75 subjects received the TAXUS® PECS. The pharmacokietics (PK) of Everolimus, delivered by the XIENCE™ V EECSS, will be performed at a minimum of 5 sites. SPIRIT II is currently in the follow-up phase.

The SPIRIT II Clinical trial first, second, and third DSMB letters are included in **Attachments 2-1**, **2-2**, and **2-3**, respectively. In addition, Guidant is providing FDA with February 7, 2006 safety reports for the SPIRIT II Clinical Trial in **Attachment 2-4**. The format of the SPIRIT II safety report is similar to the SPIRIT III monthly safety updates that are provided to FDA, however the SPIRIT II Report is presented by site.

SPIRIT III Clinical Trial

The SPIRIT III clinical trial is a collaborative effort between the US and Japan to determine the safety and efficacy of the XIENCE™ V EECSS for the treatment of subjects with a maximum of two *de novo* coronary artery lesions. Currently 870 subjects are enrolled, however enrollment is still ongoing. The study design includes a: Randomized Clinical Trial (RCT); Concurrent US 2.25 mm non-randomized arm (2.25 mm diameter stent); Concurrent US 4.0 mm non-randomized arm (4.0 mm diameter stent); Concurrent US 38 mm non-randomized arm (38 mm length stent); and Concurrent Japanese non-randomized arm. Additionally, there will be a pharmacokinetic (PK) substudy at a minimum of 5 sites in the US and a minimum of 5 sites in Japan.

To date, 123 subjects have received greater than one stent in either the first or second treated lesion. The treatment assignment is unknown, however approximately 2/3 of patients could have received multiple XIENCE™ V stents.

The DSMB concluded that the SPIRIT III study may continue without modification. The November 17, 2005 meeting minutes from the DSMB review of SPIRIT III are included in **Attachment 2-5** of this supplement. The next DSMB meeting is scheduled for March, 2006.

The safety update from SPIRIT III is identical to the safety data provided to Dr. Heather Agler (FDA) by Kendra Basler (GDT) on February 1, 2006. For ease of review, the SPIRIT III Randomized Clinical Trial Safety Report and the SPIRIT III 4.0 mm Registry Safety Report are included in this supplement in **Attachments 2-6** and **2-7**, respectively.

Guidant believes there is sufficient justification to initiate the SPIRIT IV clinical trial to continue to evaluate the safety and efficacy of XIENCE™ V EECSS and to fulfill the FDA's request in the letter dated March 6, 2005:

You have indicated in your submission that you intend to pursue a continued access registry study. While full details of such a study are not required as a precondition for approval of your current IDE study, FDA encourages you to submit your proposal early for FDA feedback and suggestions. Given clinical interest in the interventional cardiology community regarding DES performance in more complex lesions, such as multivessel stenting, FDA encourages you to consider a plan to include such subjects in a future continued access study.

3.0 Risks Posed by the Device

The risks identified are consistent with the risks included in the SPIRIT III protocol. No new risks have been identified. The SPIRIT IV risks are included in the SPIRIT IV protocol in section 2.7.1 and are also provided here for ease of review.

Potential Risks:

Risks from Cardiac Catheterization, Stenting and Percutaneous Transcatheter Coronary Angioplasty

There is extensive clinical and commercial experience worldwide with cardiac catheterization and interventional procedures and it is expected that the surgical and procedural risks will not be significantly different in this clinical trial. Adverse events that may result from stent intervention include abrupt closure, acute myocardial infarction, allergic reaction or hypersensitivity to contrast agent and drug reactions to anti-platelet drugs or contrast agent, aneurysm, arterial perforation and injury to the coronary artery, arterial rupture, arteriovenous fistula, atrial and ventricular arrhythmias (including bradycardia, tachycardia and fibrillation), bleeding complications which may require transfusions, cardiac or pulmonary or renal failure, cardiogenic shock, cardiac tamponade, coronary artery spasm, coronary artery or stent embolism, coronary artery or stent thrombosis, death, distal emboli (air, tissue or thrombotic), emergent or non-emergent coronary artery bypass graft surgery, hypertension, hypotension, infection or pain at insertion site, ischemia (myocardial), nausea and vomiting, palpitations, pericardial effusion, peripheral ischemia (due to vascular or nerve injury), pseudoaneurysm, restenosis of the stented segment of the artery, stroke/cerebrovascular accident (CVA), total occlusion of the coronary artery, unstable or stable angina pectoris, vascular complications including at the entry site which may require vessel repair including hematoma, and vessel dissection.

Associated Risks of Everolimus

Certican®, the oral formulation of everolimus developed by Novartis Pharmaceuticals Corporation has been evaluated in clinical trials. It has been approved in 47 countries outside of the United States. It is currently under review for approval in the USA. Certican® is indicated for the prophylaxis of organ rejection in adult subjects receiving an allogeneic renal or cardiac transplant, to be used in combination with cyclosporine (microemulsion formulation) and corticosteroids. Under these conditions, the following adverse events were noted in clinical trials:

Abdominal pain, acne, anemia, coagulopathy, diarrhea, edema, hemolysis, hemolytic uremic syndrome, hypercholesterolemia, hyperlipidemia, hypertension, hypertriglyceridemia, hypogonadism male, infections (wound infection, urinary tract infection, pneumonia, pyelonephritis, sepsis and other viral, bacterial and fungal infections), leukopenia, liver function test abnormality, hepatitis, hepatic disorders, lymphocele, myalgia, nausea, pneumonitis, rash, renal tubular necrosis, thrombocytopenia, venous thromboembolism, vomiting (Novartis Certican® Investigators' Brochure 2004).

The subjects that reported the adverse events noted above were receiving Certican® doses of either 1.5 mg/day or 3.0 mg/day for at least 12 months together with cyclosporine microemulsion formulation and corticosteroids. The single, one time dose of everolimus on this XIENCE V device is less than the recommended first dose that a renal transplant subject is prescribed to take. For example, in this study, a subject with a single lesion can be exposed to a maximum of 234 μg of everolimus (considering the usage of two overlapping stents, one 3.5 x 28 mm stent and one 3.5 x 8 mm stent). Assuming that the entire drug was released on day 1, the single dose of drug released into the blood would be approximately 9-18% of a single oral dose in renal transplant subjects (Assuming a bioavailability of 90% (Novartis Certican® Investigators' Brochure 2004)). A subject with two lesions can be exposed to a maximum of 468 μg of the drug everolimus (considering the usage of two overlapping stents per lesion, a 3.5 x 28 mm and a 3.5 mm x 8 mm per lesion). Assuming that the entire drug was released on day 1, the single dose of drug released into the blood would be approximately 17-35% of a single oral recommended dose in renal transplant subjects (Assuming a bioavailability of 90% (Novartis Certican® Investigators' Brochure 2004)). A subject with three lesions can be exposed to a maximum of 702 μg of the drug everolimus (considering the usage of two overlapping stents per lesion, a 3.5 x 28 mm and a 3.5 x 8 mm per lesion). Assuming that the entire drug was released on day 1, the single dose of drug released into the blood would be approximately 26-52% of a single oral recommended dose in renal transplant subjects (assuming a bioavailability of 90% (Novartis Certican® Investigators' Brochure 2004)). Additionally, if this subject were to receive a bailout stent (an 8 mm stent is recommended), he/she will be exposed to an additional drug dose of 37 or 53 μg per stent. In preclinical studies conducted at Guidant, everolimus, when delivered from a stent platform using dose formulations of 100 $\mu g/cm^2$ (XIENCE™ V EECSS), 200 $\mu g/cm^2$, 260 $\mu g/cm^2$ (slow release formulation) and 803 $\mu g/cm^2$ (maximum dose formulation), had a wide safety margin. At no time point was luminal thrombus, medial thinning, or medial necrosis observed. Additionally, studies have shown that the total dose of everolimus on the coated stent will be released over a period of three months into the surrounding tissue and circulation (Internal document - Guidant GLP Preclinical and Pharmacokinetic studies). Based on the data available from preclinical studies, safety data from on-going XIENCE V clinical trials, the maximum lesion length allowed in this study, and the available stent sizes, Guidant proposes recommending a maximum of 44 mm of stent length per lesion including a bail out stent.

Drug Interactions with Everolimus

Everolimus is extensively metabolized by the CYP3A isozyme in the gut wall and liver and is a substrate for the countertransporter P-glycoprotein. Therefore, absorption and subsequent elimination of everolimus may be influenced by drugs that affect these pathways. Everolimus has also been shown to reduce the clearance of some prescription medications when it was administered orally along with cyclosporin (CsA). Formal drug interaction studies have not been performed with XIENCE™ V EECSS. Therefore, due consideration should be given to the potential for both systemic and local drug interactions in the vessel wall when deciding to place the XIENCE™ V EECSS in a subject taking a drug with known interactions with everolimus.

Everolimus when prescribed as an oral medication may interact with the following drugs (Novartis Certican® Investigators' Brochure 2004), CYP3A isozyme inhibitors (ketoconazole, itraconazole, ritonavir, erythromycin, clarithromycin, fluconazole, calcium channel blockers), inducers of CYP3A isozyme (rifampin, rifabutin, carbamazepine, phenobarbital, phenytoin), antibiotics (ciprofloxacin, ofloxacin), glucocorticoids, HMGCoA reductase inhibitors (simvastatin, lovastatin), digoxin, cisapride (theoretical potential interaction), sildenafil (Viagra®) (theoretical potential interaction), antihistaminics (terfenadine, astemizole) and grapefruit juice.

Associated Risks of XIENCE™ V EECSS Polymer

The safety and biocompatibility of acrylic and fluoro deposited polymer coatings have been demonstrated based upon the XIENCE™ V EECSS biocompatibility testing per ISO 10993-1 and the long use of these polymers in medical implants. However, the long-term outcome of the XIENCE™ V EECSS polymer as a permanent implant is unknown at present.

Genotoxicity, Carcinogenicity and Reproductive Toxicity of XIENCE™ V EECSS

The genotoxicity, carcinogenicity and reproductive toxicity of the XIENCE™ V EECSS have not been evaluated. Everolimus when given orally in rat and mouse carcinogenicity studies, showed no oncogenic potential at doses up to 0.9 mg/kg. There was no evidence of mutagenic activity of everolimus in a variety of in vitro and in vivo tests. Reproductive organs were identified as target organs in pre-clinical toxicity studies in all animal species tested. Everolimus when given orally crosses the placenta in rats and is toxic to the fetus (Novartis Certican® Investigators' Brochure 2004).

Therefore, pregnant and nursing subjects and those planning pregnancy up to one year following the index procedure are excluded from this study. Female subjects with childbearing potential enrolled in this study must have a negative pregnancy test done within 7 days prior to the index procedure. If a female subject does get pregnant, the risks to the fetus are unknown. There are no adequate studies in men or pregnant women regarding the safety of everolimus or the XIENCE™ V EECSS. Therefore, effective contraception should be used before implanting a XIENCE™ V EECSS. The method of contraception is a personal choice but needs to be made with respect to the subject's values with adequate medical information on the effectiveness and safety of the method. Except for surgical removal of the uterus and ovaries or total abstinence, all methods of birth control have a failure rate. Intrauterine devices (IUD), hormonal contraceptives (birth control pills, injections or implants), tubal ligation or partner's vasectomy and barrier contraceptives (condoms, diaphragms, cervical caps) are available means of birth control. The primary care provider or a gynecologist should be consulted concerning the best birth control method for the subject given his/her medical history and lifestyle choices.

Risk Management Procedures

All subjects who receive a study stent will receive 75 mg of clopidogrel bisulfate (Plavix) orally daily for a minimum of 6 months to reduce the risk of stent thrombosis and to provide extended protection to compensate for potentially delayed endothelialization

after stent implant. Subjects will also receive aspirin (≥ 80 mg) orally daily to be taken throughout the length of the trial (5 years) following the procedure.

Subjects will be monitored closely throughout the trial duration. Subjects will be evaluated clinically at pre-determined time points to assess their clinical status.

An independent blinded Data Safety Monitoring Board (DSMB) will monitor safety of the subjects throughout the trial.

Potential Benefits

The restenosis rate following stenting with bare metal stents can be in excess of 40% (Narins and Topol 2003). Despite progress in the developments in coronary stenting, restenosis remains a major limiting factor in symptomatic relief for the patient and medical resource utilization, although it is not a major contributor to cardiac mortality.

Other drug eluting stents have shown a reduction in the restenosis rate when compared to metallic stents. For example, in a recent randomized clinical trial, in-segment restenosis rates were 8.9% in the drug eluting stent group vs. 36.3% in the metallic stent control group (Moses, Leon et al. 2003). Drug eluting stents have the potential to reduce restenosis and may have a positive effect on both patient outcomes and the costs of medical care. In the FUTURE trials comparing everolimus-eluting stents to metallic stents, the in-stent angiographic binary restenosis rates at 180 days were 0% in the everolimus stent group and 9.1% in the control group for FUTURE I (Grube, Gerckens et al. 2002; One-Year Report. FUTURE I Trial December 2, 2003) and 0% versus 19.4% for FUTURE II (Six-Month Report. FUTURE II Trial September 1, 2004). In the SPIRIT FIRST trial comparing the XIENCE™ V EECSS to the metallic ML VISION® stent, the in-stent angiographic restenosis rates at 180 days were 0% and 26.9% (p=0.01), respectively, highlighting the differences between treatment and control groups. The in-segment binary restenosis rates were 4.3% and 34.6% (p=0.01), respectively, for the XIENCE™ V EECSS and Control groups (180-day Progress Report. SPIRIT FIRST Clinical Trial 2004).

The long term effects and potential benefits of drug eluting stents are not yet known.

4.0 Proposed Rate of Continued Enrollment

The SPIRIT IV Clinical Trial will enroll approximately 1,125 subjects at up to 50 sites in the United States. This trial will be randomized (2:1 XIENCE™ V EECSS : TAXUS EXPRESS^2 PECS) in subjects with a maximum of three *de novo* native coronary artery lesions, maximum of two lesions per epicardial vessel with reference vessel diameters (RVD) ≥ 2.5 mm to ≤ 4.25 mm, lesion lengths ≤ 28 mm. Overlapping stents will be allowed for XIENCE™ V subjects with lesions > 22 mm.

Table 4-1: Randomization Ratio and Sample Size

Treatment Group	**XIENCE V**	**TAXUS**
Randomization Ratio	2	1
Sample Size	750	375

5.0 Clinical Protocol Summary for SPIRIT IV Trial

<table>
<tr><td>Trial Name and Number</td><td>SPIRIT IV Clinical Trial: 05-368</td></tr>
<tr><td>Objectives</td><td>To evaluate the safety and efficacy of the XIENCE™ V Everolimus Eluting Coronary Stent System (XIENCE V) for the treatment of up to three de novo native coronary artery lesions, maximum of two lesions per epicardial vessel</td></tr>
<tr><td>Study Design</td><td>Prospective, randomized, active-controlled, single-blinded, multicenter, US clinical trial evaluating XIENCE V in subjects with reference vessel diameters (RVD) ≥ 2.5 mm to ≤ 4.25 mm and lesion lengths ≤ 28 mm; non-inferiority to FDA-approved commercially available TAXUS® EXPRESS²™ Paclitaxel Eluting Coronary Stent System (TAXUS) (NOTE: RVD ≥ 2.5 mm to ≤ 3.75 mm until 4.0 mm TAXUS is commercially available)
<table>
<tr><td>Treatment Group</td><td>XIENCE V</td><td>TAXUS</td></tr>
<tr><td>Randomization Ratio</td><td>2</td><td>1</td></tr>
<tr><td>Sample Size</td><td>750</td><td>375</td></tr>
</table>
<table>
<tr><td></td><td colspan="3">Reference Vessel Diameters, Lesion Lengths, and Stent Sizes</td></tr>
<tr><td></td><td>RVD or Lesion Length</td><td>XIENCE V Sizes</td><td>TAXUS Sizes</td></tr>
<tr><td>Diameters (mm)</td><td>RVD ≥ 2.5 to ≤ 4.25*</td><td>2.5, 3.0, 3.5, 4.0*</td><td>2.5, 2.75, 3.0, 3.5, 4.0*</td></tr>
<tr><td>Lengths (mm)</td><td>Lesion Lengths ≤ 28</td><td>8, 18, 28</td><td>8, 12, 16, 20, 24, 28, 32</td></tr>
</table>
*RVD ≥ 2.5 mm to ≤ 3.75 mm and stent sizes up to 3.5 mm until 4.0 mm TAXUS is commercially available

If a subsequent generation TAXUS is released during the course of the study, it may replace the TAXUS® EXPRESS²™ Paclitaxel Eluting Coronary Stent System.</td></tr>
<tr><td>Subject Enrollment</td><td>Approximately 1,125 subjects enrolled at up to 50 sites in the United States</td></tr>
<tr><td>Subject Follow-Up</td><td>Clinical follow-up at 30, 180, 270 days, and 1, 2, 3, 4, and 5 years</td></tr>
<tr><td>Primary Endpoint</td><td>Ischemia driven target vessel failure (TVF) at 270 days</td></tr>
<tr><td>Secondary Endpoints</td><td>- Ischemia driven TVF at 30, 180 days, and 1, 2, 3, 4, and 5 years
- Ischemia driven target lesion revascularization (TLR) at 30, 180 and 270 days, and 1, 2, 3, 4, and 5 years
- Ischemia driven target vessel revascularization (TVR) at 30, 180 and 270 days, and 1, 2, 3, 4, and 5 years
- Ischemia driven major adverse cardiac event (MACE) at 30, 180 and 270 days and 1, 2, 3, 4, and 5 years
- Acute Success (clinical device and clinical procedure)</td></tr>
<tr><td>Primary Analytical Population</td><td>The primary analysis of TVF at 270 days will be performed on the intent-to-treat population. All study endpoints will be analyzed descriptively.</td></tr>
</table>

Safety Monitoring	- Data Safety Monitoring Board: Review of all adverse events - Clinical Events Committee: Review and adjudication of all safety endpoint events and vascular and bleeding events
Study Blinding	• Blinded Personnel: - Subjects - Site personnel/physician carrying out clinical follow-up - All Sponsor personnel (except those noted below under Unblinded Personnel) - Data Safety Monitoring Board - Clinical Events Committee - Angiographic core laboratory • Unblinded Personnel: - Physician placing study stent(s) - Catheterization laboratory research personnel - Sponsor biostatisticians writing and verifying randomization code, Clinical Data Architect, Information Systems personnel, Inventory Management personnel, Clinical Safety Monitors, and Site Monitors
Treatment Strategy	• Treatment of up to three *de novo* native coronary artery lesions is permitted, with a maximum of two lesions per epicardial vessel • Target lesion(s) will be treated in accordance with the randomization schedule after satisfying the general and angiographic inclusion and exclusion criteria as defined in the protocol. If more than one target lesion will be treated, all lesions must receive the treatment that has been assigned as per the randomization • Pre-dilatation of the target lesion(s) is required. Randomization will be done only after pre-dilatation is successfully completed without complications (visually estimated diameter stenosis < 50%, TIMI Grade 3 flow, post dilatation lesion length within the requirements of the protocol, and no angiographic complications or prolonged chest pain [per physician discretion]). If more than one target lesion will be treated, randomization will be done after successful and uncomplicated pre-dilatation of the first target lesion. If two target lesions in one epicardial vessel will be treated, per physician discretion, pre-dilatation may be performed on both lesions and randomization will be done only after both pre-dilatations are successfully completed without complications • Treatment of lesion(s) ≤ 28 mm in length by visual estimation. A minimum of 3 mm of non-diseased tissue on either side of the target lesion should be covered by the study stent • Treatment of target lesion(s) > 22 mm to ≤ 28 mm in length by visual estimation will be done by overlapping two 18 mm stents, or overlapping one 28 mm stent and one 8 mm stent in the XIENCE V group; overlap of a minimum of 1 mm and a maximum of 4 mm is recommended • In the case of planned stent overlap, the distal stent should be deployed first, followed by deployment of the proximal stent • In the case of two target lesions in the same epicardial vessel, the distal lesion should be treated first followed by the proximal lesion • Bailout stenting during the index procedure, if required, must use a stent from the same treatment group as assigned per the randomization • All subjects receiving a study stent will be maintained on a therapeutic daily dose of 75 mg of clopidogrel bisulfate for a minimum of 6 months and aspirin ≥ 80 mg daily to be taken throughout the length of the trial (5 years) following the index procedure. Ticlopidine hydrochloride may be given to subjects with allergic response to clopidogrel bisulfate as per the standard of care at the hospital

Key Inclusion Criteria	• Target lesion(s) must be located in a native coronary artery with visually estimated diameter of ≥ 2.5 mm to ≤ 4.25 mm; treatment of up to three *de novo* target lesions, maximum of two *de novo* target lesions per epicardial vessel (NOTE: RVD ≥ 2.5 mm to ≤ 3.75 mm until 4.0 mm TAXUS is commercially available) • Target lesion(s) must measure ≤ 28 mm in length by visual estimation • If more than one target lesion will be treated, the RVD and lesion length of each must meet the above criteria • The target lesion(s) must be in a major artery or branch with a visually estimated stenosis of ≥ 50% and < 100% with a TIMI flow of ≥ 1 • Non-study, percutaneous intervention for lesions in a target vessel (including side branches) is allowed if done ≥ 9 months prior to the index procedure • Non-study percutaneous intervention for lesions in a non-target vessel involving: - Successful and uncomplicated (visually estimated diameter stenosis < 50%, TIMI Grade-3 flow, no ECG changes, prolonged chest pain, or angiographic complications) bare-metal stent, balloon dilatation, cutting balloon, atherectomy, thrombectomy, and laser treatments are allowed if done ≥ 24 hours prior to the index procedure or during (before randomization) the index procedure. For interventions done within 24 to 48 hours prior to the index procedure, CK and CK-MB must be assessed to be < 2 times the upper limit of normal at the time of the index procedure. NOTE: Procedures within the 24 hour period preceding the index procedure are not permitted - Unsuccessful or complicated bare-metal stent, balloon dilatation, cutting balloon, atherectomy, thrombectomy, and laser treatments are allowed if done ≥ 30 days prior to the index procedure - Drug-eluting stent treatment is allowed if done ≥ 90 days prior to the index procedure • Non-study, percutaneous interventions for lesion(s) in a target vessel (including side branches) or non-target vessel are allowed if done ≥ 9 months after the index procedure
Key Exclusion Criteria	• The target lesion(s) meets any of the following criteria: - Left main coronary artery location including left main ostial location (NOTE: RCA-aorto-ostial lesions are not excluded) - Located within 2 mm of the origin of the LAD or LCX - Located within an arterial or saphenous vein graft or distal to a diseased (vessel irregularity per angiogram and any visually estimated diameter stenosis > 20%) arterial or saphenous vein graft - Involves a bifurcation in which the side branch is ≥ 2 mm in diameter AND the ostium of the side branch is > 50% stenosed by visual estimation - Involves a side branch requiring pre-dilatation - Total occlusion (TIMI flow 0) prior to wire crossing - Excessive tortuosity proximal to or within the lesion - Extreme angulation (≥ 90%) proximal to or within the lesion - Heavy calcification - Restenotic from previous intervention • Subject has received brachytherapy in any epicardial vessel (including side branches) • The target vessel contains thrombus • Another clinically significant lesion in the target vessel is present that requires or has a high probability of requiring PCI during the index procedure • Another lesion in a target or non-target vessel (including all side branches) is present that requires or has a high probability of requiring PCI within 9 months after the index procedure

Definitions	
Ischemia driven major adverse cardiac event (MACE)	The composite endpoint comprised of • Cardiac death • Myocardial infarction (MI, classified as Q-wave and non-Q wave) • Ischemia driven target lesion revascularization (TLR) by CABG or PCI
Ischemia driven target lesion revascularization (TLR)	Revascularization of a target lesion associated with any of the following • Positive functional ischemia study • Ischemic symptoms and angiographic diameter stenosis ≥ 50% by core laboratory QCA • Angiographic diameter stenosis ≥ 70% by core laboratory QCA without angina or positive functional study
Ischemia driven target vessel revascularization (TVR)	Revascularization of a lesion within the target vessel associated with any of the following • Positive functional ischemia study • Ischemic symptoms and angiographic diameter stenosis ≥ 50% by core laboratory QCA • Angiographic diameter stenosis ≥ 70% by core laboratory QCA without angina or positive functional study
Ischemia driven target vessel failure (TVF)	The composite endpoint comprised of • Cardiac death • Myocardial infarction (MI, classified as Q-wave and non-Q wave) • Ischemia driven target lesion revascularization (TLR) by CABG or PCI • Ischemia driven target vessel revascularization (TVR) by CABG or PCI
In-segment	Within the margins of the stent and 5 mm proximal and 5 mm distal to the stent
Target lesion	Lesion that has met the angiographic inclusion and exclusion criteria and that is to be treated during the index procedure.
Target vessel	The entire epicardial vessel in which the target lesion is located, including side branches

Key Inclusion Criteria	• Target lesion(s) must be located in a native coronary artery with visually estimated diameter ≥ 2.5 mm to ≤ 4.25 mm; treatment of up to three *de novo* target lesions, maximum of two *de novo* target lesions per epicardial vessel (NOTE: RVD ≥ 2.5 mm to ≤ 3.75 mm until 4.0 mm TAXUS is commercially available) • Target lesion(s) measures ≤ 28 mm in length by visual estimation • If more than one target lesion will be treated, the reference vessel diameter and lesion length of each must meet above criteria • The target lesion(s) must be in a major artery or branch with a visually estimated stenosis of ≥ 50% and < 100% with a TIMI flow of ≥ 1 • Non-study, percutaneous intervention for lesions in a target vessel is allowed if done ≥ 9 months prior to the index procedure • Non-study, percutaneous intervention for lesions in a non-target vessel involving: - Successful, uncomplicated bare-metal stent, balloon dilatation, or cutting balloon treatment is allowed any time prior to, or during (before randomization) the index procedure - Successful, uncomplicated atherectomy, thrombectomy, or laser treatment is allowed if done ≥ 24 hours prior to the index procedure - Unsuccessful, complicated bare-metal stent, balloon dilatation, cutting balloon, atherectomy, thrombectomy, or laser treatment is allowed if done ≥ 30 days prior to the index procedure - Drug-eluting stent treatment is allowed if done ≥ 90 days prior to the index procedure
Key Exclusion Criteria	• Target lesion(s) meets any of the following criteria: - Left main location including left main ostial location - Located within 2 mm of the origin of the LAD or LCX - Located within an arterial or saphenous vein graft or distal to a diseased (vessel irregularity per angiogram and > 20% stenosed lesion by visual estimation) arterial or saphenous vein graft - Involves a bifurcation in which the side branch is ≥ 2 mm in diameter and the ostium of the side branch is > 50 % stenosed by visual estimation - Involves a side branch requiring pre-dilatation - Total occlusion (TIMI flow 0) prior to wire crossing - Excessive tortuosity proximal to or within the lesion - Extreme angulation (≥ 90%) proximal to or within the lesion - Heavy calcification - Restenotic from previous intervention • Subject has received brachytherapy in any epicardial vessel (including side branches) • The target vessel contains thrombus • Another clinically significant lesion in the target vessel is present that requires or has a high probability of requiring PCI during the index procedure • Subject has a high probability that PCI for lesions in a target or non-target vessel will be required within 9 months after the index procedure

Definitions	
Ischemia driven major adverse cardiac event (MACE)	The composite endpoint comprised of • Cardiac death • Myocardial infarction (MI, classified as Q-wave and non-Q wave) • Ischemia driven target lesion revascularization (TLR) by CABG or PCI
Ischemia driven target lesion revascularization (TLR)	Revascularization at the target lesion associated with any of the following • Positive functional ischemia study • Ischemic symptoms and angiographic diameter stenosis ≥ 50% by core laboratory QCA • Revascularization of a target lesion with angiographic diameter stenosis ≥ 70% by core laboratory QCA without angina or positive functional study
Ischemia driven target vessel revascularization (TVR)	Revascularization at the target vessel associated with any of the following • Positive functional ischemia study • Ischemic symptoms and angiographic diameter stenosis ≥ 50% by core laboratory QCA • Revascularization of a target vessel with angiographic diameter stenosis ≥ 70% by core laboratory QCA without angina or positive functional study
Ischemia driven target vessel failure (TVF)	The composite endpoint comprised of • Cardiac death • Myocardial infarction (MI, classified as Q-wave and non-Q wave) • Ischemia driven target lesion revascularization (TLR) by CABG or PCI • Ischemia driven target vessel revascularization (TVR) by CABG or PCI
In-segment	Within the margins of the stent and 5 mm proximal and 5 mm distal to the stent
Target lesion	Lesion that has met the angiographic inclusion and exclusion criteria and that is to be treated during the index procedure.
Target vessel	The entire epicardial vessel in which the target lesion is located, including side branches

Note: The complete protocol for SPIRIT IV is provided in section 2.7.1 of this supplement.

6.0 Guidant's Progress in Obtaining Marketing Approval for the XIENCE™ V EECSS

The XIENCE™ V Everolimus Eluting Coronary Stent System is presently approved in 25 countries of the European Union under the XIENCE™ V Everolimus Eluting Coronary Stent System trade name.

The following is a list of countries of the European Union where the XIENCE™ V EECSS has been approved:

Austria	Belgium	Cyprus
Czech Republic	Denmark	Estonia
Finland	France	Germany
Greece	Hungary	Ireland
Italy	Latvia	Lithuania
Luxenbourg	Malta	Poland
Portugal	Slovakia	Slovenia
Spain	Sweden	The Netherlands
United Kingdom		

Guidant is ramping up manufacturing and building inventory to support the European launch of XIENCE™ V EECSS beginning in the second quarter of 2006.